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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,360	06/19/2006	Runan Mei	P71315US0	3126

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1625	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,360	MEI ET AL.	
	Examiner	Art Unit	
	Nizal S. Chandrakumar	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01/10/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *23-25 and 28-55* is/are rejected.

7)☒ Claim(s) *26-27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application filed 06/19/2006 is a 371 of PCT/CN04/01418 12/06/2004 CHINA 200310123623.X 12/19/2003 CHINA 200410044335.X 05/26/2004.

Applicant's response filed 01/10/2008 is acknowledged.

Applicants cancelled claims 1-22.

Applicants added new claims 23-55.
The scope of the original claims 1-22 and the newly presented claims 23-55 differ substantially.

Response to applicants Remarks:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 25, 29-32, 38 and 55 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite the same subject matter twice. If the ratio of S and R diol is 1, then the mixture is racemic.

Claim 29 lacks proper antecedent basis. Claim 29 depends on claim 28 which refers to a solvent; claim 29 is drawn to multi-component solvent.

In claim 30, it is unclear what C>4 ester is.

Claims 31, 32 lack proper antecedent basis. Ethers are not included in the solvent lists of the parent claims.

In claim 38, it unclear what 'sulfochloride' is.

Claim 55 recites 'routine formulation through routine methods'. It is unclear what these routine operations are.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Applicant's amendments and remarks overcome the previously presented rejections.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Applicant's remarks and amendments overcome the rejection set forth in the previous office action.

Newly presented claim 23 rejected under 35 U.S.C. 102(b) as being anticipated by Bogeso et al. (US 4943, 590).

Claim 23 is drawn to diol intermediates wherein the ratio of the optical isomers is between 0.5 and 1.5.

Bogeso et al. teach racemic diol intermediate (column 3 lines 10 and 11).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious

at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Applicant's cancellation of claims 1-22 and remarks overcome the previously presented rejections.

New Rejections:

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 23-25, 28-55 rejected under 35 U.S.C. 103(a) as being unpatentable over Bogeso et al. (US 4943, 590, US 4,650,884) , in view of Norris et al. (1924, Experimental Organic Chemistry, McGraw-Hill Book Company Inc. pages 3).

The instant claims 23-25 and 28-36 are drawn to crystalline diol intermediate (free base as well as acid salts), purification by crystallization of the diol intermediate and cyclization of the diol intermediate to citalopram as well as methods of making a drug with citalopram and its salts.

The cyclization of purified diol (as well as resolved diol) to citalopram is taught by Bogeso et al. (US 4943,590 (column 6, Example 2 and US 4,650,884, column 5, Example 2). Crystallization or organic compounds in general is taught by Norris et al. (see below). Bogeso et al.(US 4,650,884, column 4) teach purification of diol in a solid form of analytically pure acid addition salt.

The difference is that in the prior art the diol intermediate is purified in solution (see column 4, Example 1) and the solution containing the diol is subjected to cyclization reaction, while in the instant case the diol is crystallized and the crystals are dissolved in a solvent and then the solution is subjected to cyclization.

Further in the instant specification, the diol is purified as free base. The prior art does not teach all the generically claimed limitations, such as ethers for crystallization, of the instant claims.

Crystallization per se is a well known essential process in the practice of organic chemistry, See, Experimental Organic Chemistry, James F. Norris, Published 1924, page 3, "When an organic compound has been prepared it must be purified from the by-products which are formed at the same time. In the case of solid substances crystallization is ordinary used for this purpose....". One page 4 of this reference Norris lists the solvents that are commonly used in the crystallization processes.

One skilled in the art, attempting to identify alternate methods of making commercially important compounds would be motivated to prepare pure intermediates that are functionally equivalent (the diol being in solution during the cyclization process) by crystallization or any other means because it is well known in the art of organic laboratory methods that pure starting materials provide pure products, further in view of the prior art teachings of Norris et al. which teaches purification by crystallization.

Claims 37, 38 and dependent claims rejected under 35 U.S.C. 103(a) as being unpatentable over Bogeso et al. (US 4943,590 (column 6, Example 2 and US 4,650,884, column 5, Example 2).
Claim 37 and 38 and dependent claims are drawn to purification/crystallization and resolution of diol intermediates as well as of the diols to citalopram and it salts.

Bogeso et al. (US 4943,590 (column 6, Example 2) teach resolution of diol intermediate by p-toluyltartaric acid, by the formation of addition salt (non-covalent modification of the intermediate), recovering the free base of the diol intermediate and cyclization of the diol intermediate (column 7, Example 3) with methanesulfonyl chloride to citalopram. Also see the last section of column 4 for the schematic reaction of optically pure diol intermediate to cyclized product.

The difference is that the prior art does not teach crystallization procedure for the diol intermediate. The cyclization methods in the prior art and in the instant case are the same.
One skilled in the art, attempting to identify alternate methods of making commercially important compounds would be motivated to prepare pure intermediates that are functionally equivalent (being in solution during the cyclization process) by crystallization or any other means. Likewise, to one skilled in the art at the time of the instant publication, the above cited references were available for the method of purification of the diol intermediate by crystallization, method of resolution using acylated tartaric acid and method of cyclization to citalopram in a stereo controlled manner.

Claims 53-55 are drawn to pharmaceutical methods of using Citalopram (routine formulations and routine methods as per the claims). A Google search under citalopram provides over 2,710,000 hits relating to pharmaceutical use of citalopram. Bogeso et al. (US 4943,590 column 1 lines 65-68 and coulmn 2, lines 1-6) teach pharmaceutical methods of use of Citalopram.

Claims 26 and 27 are allowable.

Claims 26-27 are objected to as depending on a rejected base claim but would be allowable if rewritten in independent form.

Applicants cancelled the original claims and added new claims. The newly recited claims are drawn to subject related matter but are not the same. This necessitated new grounds for rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nizal S. Chandrakumar whose telephone number is 571-272-6202. The examiner can normally be reached on 8.30 am - 5 pm Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached at 571-272-0867 or Primary Examiner D. Margaret Seaman can be reached at 571-272-0694. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nizal S. Chandrakumar

D. MARGARET SEAMAN
PRIMARY EXAMINER